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(54) Title: MAGNETIC RESONANCE IMAGING OF METAL CONCENTRATIONS

(57) Abstract: Provided herein is a method of magnetic resonance imaging (MRI) for in vivo mapping of concentration of a target metal ion in at least one tissue using a contrast agent selectively sensitive for the amount of target metal ion where the contrast agent itself contains a non-hydrogen imaging nucleus. Also provided a method of diagnosing a disease state and of monitoring the efficacy of a therapeutic regimen to treat the disease state using the magnetic resonance imaging methods.



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A. CLAS	SSIFICATION OF SUBJECT MATTER				
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Electronic data base consulted during the international search (name of data base and ad-					
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet					
C. DOC	UMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where a	porton riste of the relevant passages	Delegant to the ST		
X	US 5, 188,816 A (SHERRY et al) 23 February 199	3 (23 02 1993) see entire de sus	Relevant to claim No.		
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Y	US 5,834,466 A (RAMASAMY et al) 10 Novembe	# 1009 (10 11 1000)			
	lines 3+.	1 1998 (10.11.1998), see column 12,	1-36		
Y	US 5,690,905 A (ZAMORA et al) 25 November 19	007 (25 11 1007)1			
	column 2.	(23.11.1997), see abstract and	1-36		
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Date of the a	ctual completion of the international search	Date of mailing of the international sear	ch report		
11 August 2003 (11.08.2003)  Name and mailing address of the ISA/US  Mail Stop PCT, Atm: ISA/US  Commissioner for Patents  Authorized officer  Michael G. Hartley  Michael G. Hartley					
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